UNITED STATES DEPARTMENT OF COMMERCE
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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/375,246	08/16/99	PERUCHO M	P-LJ-3597

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HM22/1220

EXAMINER	
SOUAYA, J	
ART UNIT	PAPER NUMBER
1655	4

DATE MAILED: 12/20/00

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No. 09/375,246	Applicant(s) Perucho et al.
	Examiner Jehanne Souaya	Group Art Unit 1655

☒ Responsive to communication(s) filed on *Aug 16, 1999*.

☐ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) *1-23* is/are pending in the application.

Of the above, claim(s) _____ is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *1-23* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐approved ☐disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). *4,5*

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

Claim Rejections - 35 USC § 112

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 1-23 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of determining a n increased or decreased risk of developing colorectal cancer by determining the relative change in the quantity of nucleic acids between cancerous and noncancerous cells, does not reasonably provide enablement for determining any clinical outcome of a subject with any cancer. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims.

The claims are broadly drawn to determining any clinical outcome of a subject with any cancer by comparing the relative change in quantity of nucleic acids between cancerous and noncancerous cells. The specification teaches that genomic instability characterizes neoplastic transformation and generates tumor cell aneuploidy (p. 1). The specification teaches that AP-PCR DNA fingerprinting was applied to the analysis of chromosal numerical changes in human colorectal cancer by measuring the genomic damage fraction of individuals (p. 15), and further

teaches correlating GDF values in a method called amplotyping which showed that losses of sequences from chromosomes 1, 4, 9, 14, and 18 occurred in about 50% of the tumors from metastatic colon cancer. The specification, however, does not teach such studies with any other type of cancer and teaches that different cancers have been found to possess different gains and losses in different chromosomes.

The art is unpredictable as to determining a clinical outcome of any cancer. Vogelstein (Trends in Genetics, 1993, vol. 9, pp 138-141) teaches that each individual cancer arises not from a single mutation, but from the accumulation of several mutations (p. 138, col 1, lines 9-12). Vogelstein teaches that 3 to 7 "hits" are required for cancer to form, and that these hits could represent insults to separate cells, but because each cancer appears to arise from a single cellular progenitor, it is more likely that they represent sequential mutations of growth regulatory gene in a single cell and its progeny (p. 138, col. 1, 2nd para). Vogelstein further teaches that not all combinations of oncogenes (a gene whose activity leads to enhanced cell growth) will transform cells, suggesting that cells have evolved several growth control circuits and that more than one circuit must be damaged before abnormal growth ensues (see p 139, col. 1, "transformation in vitro"). Vogelstien further teaches that the cellular environment can modulate the number of hits required for tumorigenicity (p. 139, col. 2, para 1). Vogelstein also teaches an example of a model for colorectal tumorigenesis (fig. 3) which shows a sequential set of mutations in growth regulatory genes that must occur before cancer develops. Vogelstien teaches that in another type of cancer, cervical cancer, progression of HPV-initiated cells to the fully malignant state requires

additional hits in genes not yet identified (p 140, col. 2, 1st para). Thus the teachings of Vogelstien illustrate the unpredictability of the art as to what is known about the mechanisms of different cancers.

Therefore, based on the lack of guidance from the specification and the unpredictability of the art with regard to determining the clinical outcome of any type of cancer, the skilled artisan would require undue experimentation to practice the invention as broadly as it is claimed. To practice the invention, the skilled artisan would have to perform a study, measuring the GDF patients with many different types of cancers to correlate a GDF with clinical outcome. Although the amount of experimentation is not in and of itself necessarily undue, the study performed by the skilled artisan to practice the invention would be replete with trial and error, and the results of such a study are unpredictable, thus constituting undue experimentation.

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 3 and 4 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 3 and 4 are indefinite in the recitation of increased risk and decreased risk as it is unclear how one would correlate that to a clinical outcome. For example, are the risk factors meant to determine risk of developing cancer?

Claim Rejections - 35 USC § 102

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

6. Claims 1-23 are rejected under 35 U.S.C. 102(a) as being anticipated by Arribas et al (J. Of Clinical Oncology, vol. 15, pp 3230-3240; 1997).

The claims are drawn to determining any clinical outcome of a subject with any cancer by comparing the relative change in quantity of nucleic acids between cancerous and noncancerous cells. Arribas teaches the assessment of genomic damage in colorectal cancer by DNA fingerprinting. Arribas teaches that 63 tumor and paired normal mucosa samples were assessed by comparative analysis of paired normal and tumor tissue DNA fingerprints by AP PCR. Arribas teaches that an index reflecting the genomic damage fraction (GDF) was obtained for each tumor and the index was used to determine molecular and clinicopathologic correlates. Arribas also teaches that the degree of genomic damage assessed by unbiased DNA fingerprinting correlates with genotypic, phenotypic and clinical variables in colorectal carcinoma and may be useful in assessing prognosis of colorectal cancer (see abstract, p. 3230, p. 3231, col.2, table 1).

7. No claims are allowable.

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner Jehanne Souaya whose telephone number is (703)308-6565. The examiner can normally be reached Monday-Thursday from 7:30 AM to 6:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones, can be reached on (703) 308-1152. The fax phone number for this Group is (703) 305-3014.

Any inquiry of a general nature should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Jehanne Souaya

Jehanne Souaya
Patent examiner
Dec. 15, 2000

W. Gary Jones
Supervisory Patent Examiner
Technology Center 1600

12/18/00